CLAIMS

What is claimed is:

1. An RNA composition that comprises at least one double strand region, wherein said double stranded region is interrupted by at least one region of non-complementarity, wherein said composition induces destruction of a target nucleic acid sequence.

2. The RNA composition of claim 1, wherein said target nucleic acid sequence is a transcript.

3. The RNA composition of claim 1, wherein said composition is substantially incapable of eliciting an interferon pathway in a cell.

4. The RNA composition of claim 1, wherein said composition comprises one RNA molecule.

5. The RNA composition of claim 1, wherein said composition comprises two or more RNA molecules.

6. The RNA composition of claim 1, wherein said composition is further defined as comprising a construct, said construct having in a 5′ to 3′ orientation:

   a first double stranded RNA region;

   a first region of non-complementarity;

   a second double stranded RNA region;

   a second region of non-complementarity; and

   a third double stranded RNA region.

7. The composition of claim 6, wherein said RNA composition comprises at least one regulatory sequence operably linked to the construct.

8. The composition of claim 7, wherein the regulatory sequence is a constitutive promoter, an inducible promoter, a tissue-specific promoter, or a combination thereof.

9. The RNA composition of claim 1, wherein said one or more double stranded RNA regions are at least about 22 nucleotides in length.

10. The RNA composition of claim 1, wherein said one or more double stranded RNA regions are between about 22 and about 30 nucleotides in length.

11. The RNA composition of claim 1, wherein said one or more double stranded RNA regions are between about 27 and about 30 nucleotides in length.

12. The RNA composition of claim 1, wherein said one or more regions of non-complementarity are at least about 5 nucleotides in length.

13. The RNA composition of claim 1, wherein said one or more regions of non-complementarity are from about 5 to about 12 nucleotides in length.

14. The RNA composition of claim 1, wherein said one or more double stranded RNA regions are complementary to a target nucleic acid sequence.

15. The RNA composition of claim 14, wherein said one or more double stranded RNA regions are complementary to the same target nucleic acid sequence.

16. The RNA composition of claim 14, wherein said one or more double stranded RNA regions are complementary to different target nucleic acid sequences.

17. The RNA composition of claim 14, wherein said one or more double stranded RNA regions are fully complementary to a target nucleic acid sequence.

18. The RNA composition of claim 14, wherein said one or more double stranded RNA regions are complementary to a 5′ region of a target transcript.

19. The RNA composition of claim 18, wherein said 5′ region is a 5′ untranslated region of a target transcript.

20. The RNA composition of claim 14, wherein said one or more double stranded RNA regions are complementary to a 3′ region of a target transcript.

21. The RNA composition of claim 20, wherein said 3′ region is a 3′ untranslated region of a target transcript.

22. The RNA composition of claim 1, wherein said composition is encoded by a single transgene.

23. The RNA composition of claim 5, wherein said composition is encoded by two transgenes.

24. The RNA composition of claim 1, wherein the junction between at least one double stranded RNA region and at least one region of non-complementarity comprises at least two consecutive T's.

25. The RNA composition of claim 1, wherein said composition is further defined as comprising n number of double stranded regions and n-1 number of regions of non-complementarity.

26. A vector comprising the RNA composition of claim 1.

27. A transgene comprising the RNA composition of claim 1.

28. A mammalian cell comprising the RNA composition of claim 1.

29. A transgenic, non-human animal having at least one cell comprising a transgene encoding a RNA composition of claim 1, wherein the transgene is expressed in one or more cells of the transgenic animal, resulting in inducing destruction of at least one target nucleic acid sequence by the RNA composition.

30. An RNA composition comprising two or more double strand regions, adjacent regions of which are separated from each other by one or more regions of non-complementarity, wherein at least two of said double strand regions are complementary to at least two different target transcripts, wherein said RNA composition is capable of inducing destruction of said transcripts.

31. The RNA composition of claim 30, wherein said double stranded regions are fully complementary to said transcripts.

32. A vector having a promoter that operably regulates sequence that encodes an RNA, wherein said sequence comprises one or more nucleic acid sequence constructs each of which are flanked by at least two restriction enzyme sites, wherein upon intramolecular hybridization of said RNA, at least one of said constructs generates a region of non-complementarity within said RNA.

33. The vector of claim 32, wherein said two restriction enzyme sites are non-identical.

34. The vector of claim 32, wherein said sequence comprises a signal for poly (A) addition.

35. The vector of claim 32, wherein said sequence is further defined as having the following components present in a 5′ to 3′ orientation:

    a) a first restriction enzyme site;

    b) a second restriction enzyme site;

c) sequence that encodes one strand of a first region of non-complementarity;

d) a third restriction enzyme site;

e) a fourth restriction enzyme site;

f) sequence that encodes one strand of a second region of non-complementarity;

g) a fifth restriction enzyme site;

h) a sixth restriction enzyme site;

i) sequence that encodes one strand of a third region of non-complementarity;

j) a loop region;

k) sequence that encodes a second strand of the third region of non-complementarity, wherein the sequence is non-complementary to the sequence in i);

l) a seventh restriction enzyme site;

m) an eighth restriction enzyme site;

n) sequence that encodes a second strand of the second region of non-complementarity, wherein the sequence is non-complementary to the sequence in f);

o) a ninth restriction enzyme site;

p) a tenth restriction enzyme site;

q) sequence that encodes a second strand of the first region of non-complementarity, wherein the sequence is non-complementary to the sequence in c); and

r) sequence that directs addition of a poly A tail.

36. A kit comprising the vector of claim 32.

37. The kit of claim 36, wherein said kit further comprises one or more restriction enzymes.

38. The kit of claim 37, wherein said kit further comprises a buffer suitable for at least one restriction enzyme.

39. A eukaryotic cell exhibiting a target nucleic acid sequence-specific knockout phenotype, wherein said cell is transfected with at least one RNA composition capable of and under conditions suitable for inducing destruction of the target nucleic acid sequence, wherein the RNA composition comprises at least one double stranded region interrupted by at least one region of non-complementarity.

40. The cell of claim 39, wherein said cell is in a eukaryotic non-human organism.

41. An isolated genetic construct that is capable of inducing destruction of at least one target nucleic acid sequence in an animal cell that is transfected with said construct, wherein the genetic construct comprises nucleic acid sequence comprising or encoding a RNA composition, said RNA composition comprising:

a first double strand region that is substantially identical to at least a region of a first target nucleic acid sequence; and

a second double strand region that is substantially identical to at least a region of a second target nucleic acid sequence, said first and second double stranded regions separated by a region of non-complementarity, and wherein the double strand regions are under the control of at least one operable promoter.

42. The construct of claim 41, wherein the first and second target nucleic acid sequences are transcripts from the same gene or locus.

43. The construct of claim 41, wherein the first and second target nucleic acid sequences are transcripts from a different gene or locus.

44. The construct of claim 41, wherein said first and second double stranded regions are under the control of different operable promoters.

45. A method of inducing destruction of a target nucleic acid sequence in an animal cell, comprising expressing in said animal cell a genetic construct of claim 41.

46. A method of inducing destruction of at least one target nucleic acid sequence in a cell, comprising introducing to the cell an effective amount of a RNA composition comprising one or more double stranded RNA regions each of which are substantially identical to a portion of a target nucleic acid sequence, and each of which said double stranded regions are separated by the adjacent double stranded RNA region by a region of non-complementarity, wherein upon said introducing said RNA composition to the cell, said composition induces destruction of said target nucleic acid sequence.

47. The method of claim 46, wherein the cell is in a mammal.

48. The method of claim 47, wherein the mammal is a mouse.

49. A method of preparing an RNA composition of claim 1, comprising the steps of:

synthesizing two RNA strands, wherein said RNA strands are capable of forming a double stranded RNA molecule; and

combining the synthesized RNA strands under conditions wherein a double stranded RNA molecule is produced, said double stranded RNA molecule capable of inducing destruction of a target nucleic acid sequence.

50. The method of claim 49, wherein said RNA strands are chemically synthesized.

51. The method of claim 49, wherein said RNA strands are enzymatically synthesized.

52. The method of claim 49, wherein said combining step occurs in a cell following introduction into the cell of the two RNA strands or nucleic acids encoding them.

53. A method of preparing a single stranded RNA composition of claim 1, comprising the steps of:

obtaining at least one region of a nucleic acid encoding said RNA composition;

obtaining at least another region of a nucleic acid encoding said RNA composition;

cloning said regions operably together in a vector to produce a single transgene, wherein said vector comprises at least one regulatory sequence operably linked to said transgene; and

expressing said RNA composition.

54. A method of mediating RNA interference of a nucleic acid sequence in a cell or organism, comprising:

introducing into the cell or organism at least one RNA composition, wherein the RNA composition comprises in a 5′ to 3′ direction at least:

a first double stranded region;
a region of non-complementarity; and
a second double stranded region, wherein at least one of the double stranded regions targets the nucleic acid sequence for degradation; and

maintaining the cell or organism under conditions wherein degradation of the target nucleic acid sequence occurs.

55. The method of claim 54, wherein said nucleic acid sequence encodes a cellular mRNA or a viral mRNA.

56. A method of inducing destruction of nucleotide sequence from more than one locus, comprising:

introducing into the cell or organism at least one RNA composition, wherein the RNA composition comprises in a 5′ to 3′ direction at least:

a first double stranded region;
a region of non-complementarity; and
a second double stranded region, wherein the double stranded regions target different nucleic acid sequences for degradation; and

maintaining the cell or organism under conditions wherein the nucleotide sequences are destroyed.

57. The method of claim 56, wherein said method is further defined as destroying a transcript from more than one gene.